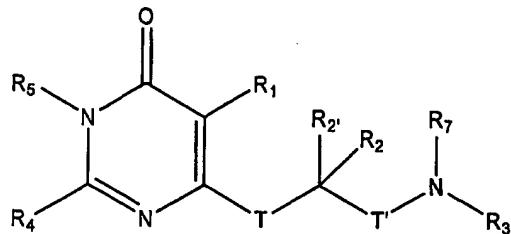


What is claimed is:

1. A compound selected from the group represented by Formula I:



Formula I

wherein:

T and T' are independently a covalent bond or optionally substituted lower alkylene;

R_1 is chosen from hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heteroaralkyl;

R_2 and $R_{2'}$ are independently chosen from hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heteroaralkyl; or R_2 and $R_{2'}$ taken together form an optionally substituted 3- to 7-membered ring;

R_3 is chosen from hydrogen, optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heteroaryl-, optionally substituted heteroaralkyl-, $-C(O)-R_6$, and $-S(O)_2-R_{6a}$;

R_4 is independently chosen from hydrogen, optionally substituted alkyl, optionally substituted alkoxy, hydroxyl, nitro, cyano, dialkylamino, alkylsulfonyl, alkylsulfonamido, alkylthio, carboxyalkyl, carboxamido, aminocarbonyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaralkyl and optionally substituted heteroaryl; and

R_5 is hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, or optionally substituted heteroaralkyl; or

R_4 taken together with R_5 form an optionally substituted 5 to 7-membered ring nitrogen-containing heterocycle, which optionally incorporates from one to two additional heteroatoms, selected from N, O, and S in the heterocycle ring;

R_6 is chosen from hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, optionally substituted heteroaralkyl, $R_{11}O$ - and $R_{12}-NH$ -;

R_{6a} is chosen from optionally substituted alkyl, optionally substituted aryl, optionally substituted alkylaryl, optionally substituted heteroaryl, optionally substituted alkylheteroaryl, and $R_{12}-NH$ -;

R_7 is chosen from hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heteroaralkyl;

or R_7 taken together with R_3 , and the nitrogen to which they are bound, form an optionally substituted 5- to 12-membered nitrogen-containing heterocycle, which optionally incorporates from one to two additional heteroatoms, selected from N, O, and S in the heterocycle ring;

or R_7 taken together with R_2 form an optionally substituted 5- to 12-membered nitrogen-containing heterocycle, which optionally incorporates from one to two additional heteroatoms, selected from N, O, and S in the heterocycle ring;

R_{11} is chosen from optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heteroaralkyl; and

R_{12} is chosen from hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heteroaralkyl;

a pharmaceutically acceptable salt of a compound of Formula I;

a pharmaceutically acceptable solvate of a compound of Formula I; or

a pharmaceutically acceptable solvate of a pharmaceutically acceptable salt of a compound of Formula I.

2. A compound of claim 1 comprising one or more of the following:

one of T and T' is absent and the other is optionally substituted alkylene;

R_1 is selected from optionally substituted lower alkyl, optionally substituted aryl, or

optionally substituted aralkyl;

R₂ is optionally substituted C₁-C₄ alkyl;

R₂' is hydrogen or optionally substituted C₁-C₄ alkyl;

R₃ is -C(O)R₆;

R₆ is selected from optionally substituted C₁-C₈ alkyl, optionally substituted aryl-C₁-C₄-alkyl-, optionally substituted heteroaryl-C₁-C₄-alkyl-, optionally substituted heteroaryl, optionally substituted aryl, R₁₁O- and R₁₂NH-;

R₁₁ is chosen from optionally substituted C₁-C₈ alkyl and optionally substituted aryl;

R₁₂ is chosen from hydrogen, optionally substituted C₁-C₈ alkyl and optionally substituted aryl;

R₇ is chosen from hydrogen, C₁-C₄ alkyl; cyclohexyl; phenyl substituted with hydroxyl, C₁-C₄ alkoxy or C₁-C₄ alkyl; benzyl; and R₁₆-alkylene-;

R₁₆ is hydroxyl, carboxy, (C₁-C₄ alkoxy)carbonyl-, di(C₁-C₄ alkyl)amino-, (C₁-C₄ alkyl)amino-, amino, (C₁-C₄ alkoxy)carbonylamino-, C₁-C₄ alkoxy-, or optionally substituted N-heterocyclyl- (particularly azetidinyl, morpholinyl, pyridinyl, indolyl, furanyl, pyrrolidinyl, piperidinyl or imidazolyl, each of which may be optionally substituted);

R₄ is chosen from hydrogen, hydroxyl, lower alkyl (particularly methyl), lower alkoxy (particularly methoxy) and cyano; and

R₅ is chosen from hydrogen, lower alkyl (particularly methyl), and aralkyl (particularly benzyl).

3. A compound of claim 2 comprising one or more of the following:

T and T' are absent;

R₁ is chosen from ethyl, propyl, methoxyethyl, naphthyl, phenyl, bromophenyl, chlorophenyl, methoxyphenyl, ethoxyphenyl, tolyl, dimethylphenyl, chlorofluorophenyl, methylchlorophenyl, ethylphenyl, phenethyl, benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, hydroxybenzyl, dichlorobenzyl, dimethoxybenzyl, naphthylmethyl, and (ethoxycarbonyl)ethyl;

R₂ is hydrogen;

R₂ is optionally substituted C₁-C₄ alkyl;

R₆ is chosen from phenyl; phenyl substituted with one or more of the following substituents: halo; C₁-C₄ alkyl; C₁-C₄ alkyl substituted with hydroxy (e.g., hydroxymethyl); C₁-C₄ alkoxy; C₁-C₄ alkyl substituted with C₁-C₄ alkoxy, halo, nitro, formyl, carboxy,

cyano, methylenedioxy, ethylenedioxy, acyl (e.g., acetyl), -N-acyl (e.g., N-acetyl) or trifluoromethyl; benzyl; phenoxyethyl-; halophenoxyethyl-; phenylvinyl-; heteroaryl-; heteroaryl- substituted with C₁-C₄ alkyl or C₁-C₄ alkyl substituted with halo (e.g., CF₃); C₁-C₄ alkyl substituted with C₁-C₄ alkoxy-; and benzyloxymethyl-;

R₇ is chosen from hydrogen, methyl, ethyl, propyl, butyl, cyclohexyl, carboxyethyl, carboxymethyl, methoxyethyl, hydroxyethyl, hydroxypropyl, dimethylaminoethyl, dimethylaminopropyl, diethylaminoethyl, diethylaminopropyl, aminopropyl, methylaminopropyl, 2,2-dimethyl-3-(dimethylamino)propyl, aminoethyl, aminobutyl, aminopentyl, aminohexyl, isopropylaminopropyl, diisopropylaminoethyl, 1-methyl-4-(diethylamino)butyl, (t-Boc)aminopropyl, hydroxyphenyl, benzyl, methoxyphenyl, methylmethoxyphenyl, dimethylphenyl, tolyl, ethylphenyl, (oxopyrrolidinyl)propyl, (methoxycarbonyl)ethyl, benzylpiperidinyl, pyridinylethyl, pyridinylmethyl, morpholinylethyl morpholinylpropyl, piperidinyl, azetidinylmethyl, azetidinylethyl, azetidinylpropyl pyrrolidinylethyl, pyrrolidinylpropyl, piperidinylmethyl, piperidinylethyl, imidazolylpropyl, imidazolylethyl, (ethylpyrrolidinyl)methyl, (methylpyrrolidinyl)ethyl, (methylpiperidinyl)propyl, (methylpiperazinyl)propyl, furanyl methyl and indolylethyl; and

R₄ is hydrogen, optionally substituted alkyl, optionally substituted aryl, alkoxy, cyano, substituted amino, carbamyl, aryloxy, heteroaryloxy, heteroaryl, optionally substituted N-heterocyclyl, or trifluoromethyl.

4. A compound of claim 3 comprising one or more of the following:

R₁ is chosen from ethyl, propyl, methoxyethyl, naphthyl, phenethyl, benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, hydroxybenzyl, dichlorobenzyl, dimethoxybenzyl, naphthylmethyl, and (ethoxycarbonyl)ethyl;

R₂ is chosen from methyl, ethyl, propyl, butyl, methylthioethyl, methylthiomethyl, aminobutyl, (CBZ)aminobutyl, cyclohexylmethyl, benzyloxymethyl, methylsulfinylethyl, methylsulfinylmethyl, and hydroxymethyl;

R₆ is chosen from phenyl, halophenyl, dihalophenyl, cyanophenyl, halo(trifluoromethyl)phenyl, hydroxymethyl-phenyl, methoxymethylphenyl, methoxyphenyl, ethoxyphenyl, carboxyphenyl, formylphenyl, ethylphenyl, tolyl, methylenedioxyphenyl, ethylenedioxypheyl, methoxychlorophenyl, methylhalophenyl, trifluoromethylphenyl, furanyl, C₁-C₄ alkyl substituted furanyl, trifluoromethylfuranyl, C₁-C₄ alkyl substituted trifluoromethylfuranyl, benzofuranyl, thiophenyl, C₁-C₄ alkyl substituted thiophenyl,

benzothiophenyl, benzothiadiazolyl, pyridinyl, indolyl, methylpyridinyl, trifluoromethylpyridinyl, pyrrolyl, quinolinyl, picolinyl, pyrazolyl, C₁-C₄ alkyl substituted pyrazolyl, N-methyl pyrazolyl, C₁-C₄ alkyl substituted N-methyl pyrazolyl, C₁-C₄ alkyl substituted pyrazinyl, C₁-C₄ alkyl substituted isoxazolyl, benzoisoxazolyl, morpholinomethyl, methylthiomethyl, methoxymethyl, N-methyl imidazolyl, and imidazolyl;

R₇ is R₁₆-alkylene-; and

R₁₆ is amino, C₁-C₄ alkylamino-, di(C₁-C₄ alkyl)amino-, C₁-C₄ alkoxy-, hydroxyl, or N-heterocyclyl.

5. A compound of claim 4 comprising one or more of the following:

R₁ is benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, or hydroxybenzyl;

R₂ is ethyl or propyl;

R₆ is optionally substituted phenyl (especially, tolyl, halophenyl, methylhalophenyl, hydroxymethyl-phenyl, halo(trifluoromethyl)phenyl-, methylenedioxyphenyl, formylphenyl or cyanophenyl); and

R₁₆ is amino.

6. A compound of claim 1 comprising one or more of the following:

one of T and T' is absent and the other is optionally substituted alkylene;

R₁ is selected from optionally substituted lower alkyl, optionally substituted aryl, or optionally substituted aralkyl;

R₂ is optionally substituted C₁-C₄ alkyl;

R₂' is hydrogen or optionally substituted C₁-C₄ alkyl;

R₃ is -C(O)R₆;

R₆ is selected from optionally substituted C₁-C₈ alkyl, optionally substituted aryl-C₁-C₄-alkyl-, optionally substituted heteroaryl-C₁-C₄-alkyl-, optionally substituted heteroaryl, optionally substituted aryl, R₁₁O- and R₁₂-NH-;

R₁₁ is chosen from optionally substituted C₁-C₈ alkyl and optionally substituted aryl;

R₁₂ is chosen from hydrogen, optionally substituted C₁-C₈ alkyl and optionally substituted aryl;

R₇ is chosen from hydrogen, C₁-C₄ alkyl; cyclohexyl; phenyl substituted with hydroxyl, C₁-C₄ alkoxy or C₁-C₄ alkyl; benzyl; and R₁₆-alkylene-;

R_{16} is hydroxyl, carboxy, (C_1 - C_4 alkoxy)carbonyl-, di(C_1 - C_4 alkyl)amino-, (C_1 - C_4 alkyl)amino-, amino, (C_1 - C_4 alkoxy)carbonylamino-, C_1 - C_4 alkoxy-, or optionally substituted N-heterocyclyl- (particularly azetidinyl, morpholinyl, pyridinyl, indolyl, furanyl, pyrrolidinyl, piperidinyl or imidazolyl, each of which may be optionally substituted; and

R_4 and R_5 taken together form an optionally substituted 5 to 7-membered nitrogen-containing heterocycle which optionally incorporates from one to two additional heteroatoms, selected from N, O, and S in the heterocycle ring.

7. A compound of claim 6 comprising one or more of the following:

T and T' are absent;

R_1 is chosen from ethyl, propyl, methoxyethyl, naphthyl, phenyl, bromophenyl, chlorophenyl, methoxyphenyl, ethoxyphenyl, tolyl, dimethylphenyl, chlorofluorophenyl, methylchlorophenyl, ethylphenyl, phenethyl, benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, hydroxybenzyl, dichlorobenzyl, dimethoxybenzyl, naphthylmethyl, and (ethoxycarbonyl)ethyl;

R_2 is hydrogen;

R_2 is optionally substituted C_1 - C_4 alkyl;

R_6 is chosen from phenyl; phenyl substituted with one or more of the following substituents: halo; C_1 - C_4 alkyl; C_1 - C_4 alkyl substituted with hydroxy (e.g., hydroxymethyl); C_1 - C_4 alkoxy; C_1 - C_4 alkyl substituted with C_1 - C_4 alkoxy, halo, nitro, formyl, carboxy, cyano, methylenedioxy, ethylenedioxy, acyl (e.g., acetyl), -N-acyl (e.g., N-acetyl) or trifluoromethyl; benzyl; phenoxyethyl-; halophenoxyethyl-; phenylvinyl-; heteroaryl-; heteroaryl- substituted with C_1 - C_4 alkyl or C_1 - C_4 alkyl substituted with halo (e.g., CF_3); C_1 - C_4 alkyl substituted with C_1 - C_4 alkoxy-; and benzyloxymethyl-;

R_7 is chosen from hydrogen, methyl, ethyl, propyl, butyl, cyclohexyl, carboxyethyl, carboxymethyl, methoxyethyl, hydroxyethyl, hydroxypropyl, dimethylaminoethyl, dimethylaminopropyl, diethylaminoethyl, diethylaminopropyl, aminopropyl, methylaminopropyl, 2,2-dimethyl-3-(dimethylamino)propyl, aminoethyl, aminobutyl, aminopentyl, aminohexyl, isopropylaminopropyl, diisopropylaminoethyl, 1-methyl-4-(diethylamino)butyl, (t-Boc)aminopropyl, hydroxyphenyl, benzyl, methoxyphenyl, methylmethoxyphenyl, dimethylphenyl, tolyl, ethylphenyl, (oxopyrrolidinyl)propyl, (methoxycarbonyl)ethyl, benzylpiperidinyl, pyridinylethyl, pyridinylmethyl, morpholinylethyl, morpholinylpropyl, piperidinyl, azetidinylmethyl, azetidinylethyl, azetidinylpropyl

pyrrolidinylethyl, pyrrolidinylpropyl, piperidinylmethyl, piperidinylethyl, imidazolylpropyl, imidazolylethyl, (ethylpyrrolidinyl)methyl, (methylpyrrolidinyl)ethyl, (methylpiperidinyl)propyl, (methylpiperazinyl)propyl, furanymethyl and indolylethyl; and

R₄ and R₅ taken together form an optionally substituted pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, piperidinyl, piperazinyl, hexahdropyrimidinyl, piperazinyl, morpholinyl, pyrrolyl, pyrazolyl, imidazolyl, dihydroisoxazolyl, or dihydrooxazolyl ring.

8. A compound of claim 1 comprising one or more of the following:

one of T and T' is absent and the other is optionally substituted alkylene;

R₁ is selected from optionally substituted lower alkyl, optionally substituted aryl, or optionally substituted aralkyl;

R₂ is optionally substituted C₁-C₄ alkyl;

R₂ is hydrogen or optionally substituted C₁-C₄ alkyl;

R₃ taken together with R₇ and the nitrogen to which they are bound, forms an optionally substituted imidazolyl; and

R₄ is chosen from hydrogen, hydroxyl, lower alkyl, lower alkoxy and cyano; and R₅ is chosen from hydrogen, lower alkyl, and aralkyl; or R₄ and R₅ taken together form an optionally substituted 5 to 7-membered nitrogen-containing heterocycle which optionally incorporates from one to two additional heteroatoms, selected from N, O, and S in the heterocycle ring.

9. A compound of claim 1 comprising one or more of the following:

one of T and T' is absent and the other is optionally substituted alkylene;

R₁ is selected from optionally substituted lower alkyl, optionally substituted aryl, or optionally substituted aralkyl;

R₂ is optionally substituted C₁-C₄ alkyl;

R₂ is hydrogen or optionally substituted C₁-C₄ alkyl;

R₃ taken together with R₇ and the nitrogen to which they are bound, forms an optionally substituted imidazolyl; and

R₄ is chosen from hydrogen, hydroxyl, lower alkyl, lower alkoxy and cyano; and R₅ is chosen from hydrogen, lower alkyl, and aralkyl; or R₄ and R₅ taken together form an optionally substituted 5 to 7-membered nitrogen-containing heterocycle which optionally incorporates from one to two additional heteroatoms, selected from N, O, and S in the heterocycle ring.

10. A compound of claim 1 comprising one or more of the following:
one of T and T' is absent and the other is optionally substituted alkylene;
R₁ is selected from optionally substituted lower alkyl, optionally substituted aryl, or
optionally substituted aralkyl;
R₂ is optionally substituted C₁-C₄ alkyl;
R₂ is hydrogen or optionally substituted C₁-C₄ alkyl;
R₃ taken together with R₇ and the nitrogen to which they are bound, forms an
optionally substituted diazepinone; and
R₄ is chosen from hydrogen, hydroxyl, lower alkyl, lower alkoxy and cyano; and R₅ is
chosen from hydrogen, lower alkyl, and aralkyl; or R₄ and R₅ taken together form an optionally
substituted 5 to 7-membered nitrogen-containing heterocycle which optionally incorporates from
one to two additional heteroatoms, selected from N, O, and S in the heterocycle ring.

11. A compound of claim 1 wherein:
R₁ is benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, or
hydroxybenzyl;
R₂ is hydrogen;
R₂ is optionally substituted C₁-C₄ alkyl;
R₃ is -C(O)R₆;
R₆ is optionally substituted phenyl;
R₇ is R₁₆-alkylene-;
R₁₆ is amino, C₁-C₄ alkylamino-, di(C₁-C₄ alkyl)amino-, C₁-C₄ alkoxy-, hydroxyl, or
N-heterocyclyl;
R₄ is chosen from hydrogen, hydroxyl, lower alkyl (particularly methyl), lower alkoxy
(particularly methoxy) and cyano; and
R₅ is chosen from hydrogen, lower alkyl (particularly methyl), and aralkyl
(particularly benzyl).

12. A compound of claim 1 wherein:
R₁ is benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, or
hydroxybenzyl;
R₂ is hydrogen;
R₂ is optionally substituted C₁-C₄ alkyl;

R₃ is -C(O)R₆;

R₆ is R₁₂NH-;

R₁₂ is chosen from hydrogen, C₁-C₄ alkyl; cyclohexyl; and optionally substituted phenyl;

R₇ is R₁₆-alkylene-,

R₁₆ is amino, C₁-C₄ alkylamino-, di(C₁-C₄ alkyl)amino-, C₁-C₄ alkoxy-, hydroxyl, or N-heterocyclyl;

R₄ is chosen from hydrogen, hydroxyl, lower alkyl (particularly methyl), lower alkoxy (particularly methoxy) and cyano; and

R₅ is chosen from hydrogen, lower alkyl (particularly methyl), and aralkyl (particularly benzyl).

13. A compound of claim 1 wherein:

R₁ is benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, cyanobenzyl, or hydroxybenzyl;

R₂ is hydrogen;

R₂ is optionally substituted C₁-C₄ alkyl;

R₃ is -C(O)R₆;

R₆ is R₁₁O-;

R₁₁ is chosen from optionally substituted C₁-C₈ alkyl and optionally substituted aryl;

R₇ is R₁₆-alkylene-;

R₁₆ is amino, C₁-C₄ alkylamino-, di(C₁-C₄ alkyl)amino-, C₁-C₄ alkoxy-, hydroxyl, or N-heterocyclyl;

R₄ is chosen from hydrogen, hydroxyl, lower alkyl (particularly methyl), lower alkoxy (particularly methoxy) and cyano; and

R₅ is chosen from hydrogen, lower alkyl (particularly methyl), and aralkyl (particularly benzyl).

14. A compound of claim 1 that is

N-(3-Amino-propyl)-N-[1-(5-benzyl-2-methyl-6-oxo-1,6-dihydro-pyrimidin-4-yl)-2-methyl-propyl]-4-methyl-benzamide;

N-(3-Amino-propyl)-N-[1-(5-benzyl-1,2-dimethyl-6-oxo-1,6-dihydro-pyrimidin-4-yl)-2-methyl-propyl]-4-methyl-benzamide;

N-(3-Amino-propyl)-N-[1-(3-benzyl-4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl)-2-methyl-propyl]-4-methyl-benzamide; or

N-(3-Amino-propyl)-N-[1-(3-benzyl-8-chloro-4-oxo-4H-pyrido[1,2-a]pyrimidin-2-yl)-2-methyl-propyl]-4-methyl-benzamide.

15. A compound of any of the above claims wherein the stereogenic center to which R₂ and R_{2'} is attached is of the R configuration.

16. A composition comprising a pharmaceutical excipient and a compound, salt, or solvate thereof of any one of claims 1-14.

17. A composition according to claim 16, wherein said composition further comprises a chemotherapeutic agent other than a compound of Formula I or a pharmaceutical salt or solvate thereof.

18. A composition according to claim 17 wherein said composition further comprises a taxane.

19. A composition according to claim 17, wherein said composition further comprises a vinca alkaloid.

20. A composition according to claim 17, wherein said composition further comprises a topoisomerase I inhibitor.

21. A method of modulating KSP kinesin activity which comprises contacting said kinesin with an effective amount of a compound according to any one of claims 1 to 13, or a pharmaceutically acceptable salt or solvate thereof.

22. A method of inhibiting KSP which comprises contacting said kinesin with an effective amount of a compound according to any one of claims 1 to 13, or a pharmaceutically acceptable salt or solvate thereof.

23. A method for the treatment of a cellular proliferative disease comprising

administering to a subject in need thereof a compound according to any one of claims 1-13, or a pharmaceutically acceptable salt or solvate thereof.

24. A method for the treatment of a cellular proliferative disease comprising administering to a subject in need thereof a composition according to any one of claims 16-20.

25. A method according to claim 23 or claim 24 wherein said disease is selected from the group consisting of cancer, hyperplasias, restenosis, cardiac hypertrophy, immune disorders, and inflammation.

26. The use, in the manufacture of a medicament for treating cellular proliferative disease, of a compound according to any one of claims 1-13, or a pharmaceutically acceptable salt or solvate thereof

27. The use of a compound as defined in claim 26 for the manufacture of a medicament for treating a disorder associated with KSP kinesin activity.